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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

| EXAMINER | |
|---|---|
| BABIC, CHRISTOPHER M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1637 | |

DATE MAILED: 09/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/621,329 | MORI ET AL. | |
| | Examiner | Art Unit | |
| | Christopher M. Babic | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 12/4/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



SDO

## DETAILED ACTION

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

**1. Claims 1-18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-2 of copending Application 10/305,110, Claims 1-18 of copending Application No. 10/621,412, and Claims 1-20 of copending Application No. 10/621,715, in view of Tam (U.S. 5,741,647).**

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F. 2d 887, 225 USPQ 645 (fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because each set of claims is drawn to a method for separating and purifying a nucleic acid wherein each method encompasses the same general inventive concept of adsorbing and desorbing a nucleic acid onto a solid phase, wherein the solid phase has hydroxyl groups on the surface thereof.

Regarding copending Application '110, Claims 1 and 2 recite the same general inventive concept of the instant application with the exception of, in the instant application, the inclusion of a membrane (i.e. solid phase) with a broad thickness range. The inclusion of this limitation is well within the range of ordinary skill in the art as demonstrated, for example, by Tam (Column 2, Lines 25-35). Claims 1 and 2 fall entirely within the scope of the instant application.

Regarding copending Application '412, Claims 1-3 recite the same general inventive concept of the instant application with the exception of, in the instant application, the inclusion of a membrane (i.e. solid phase) with a broad thickness range. The inclusion of this limitation is well within the range of ordinary skill in the art as demonstrated, for example, by Tam (Column 2, Lines 25-35). Claims 1-3 fall entirely within the scope of the instant application.

Regarding copending Application '715, Claim 1 recites recite the same general inventive concept of the instant application with the exception of, in the instant

application, the inclusion of a membrane (i.e. solid phase) with a broad thickness range. The inclusion of this limitation is well within the range of ordinary skill in the art as demonstrated, for example, by Tam (Column 2, Lines 25-35). Claim 1 falls entirely within the scope of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**1. Claims 9, 17, and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

A) Regarding Claim 9, the phrase "the nucleic acid in a sample solution" lacks proper antecedent basis, because while the claim previously refers to a nucleic acid, it does not previously refer to a nucleic acid in a sample solution.

B) Regarding Claims 17 and 18, the claims are indefinite because they recite a long series of method steps but they do not clearly relate these method steps to the method steps that are already present in Claim 1 from which these two claims depend.

That is, it is not clear if these steps result in the adsorbing and desorbing required in Claim 1 or if they are additional steps to be practiced along with those steps of Claim 1. The method steps recited in claims 17 and 18 never clearly recite or are correlated to the adsorbing and desorbing of claim 1.

C) Claim 17 is further indefinite in part (c) of the claim because it recites discharging the sample solution "containing nucleic acids" out of the container. It is confusing because it is unclear how the method results in isolation of nucleic acids if the solution containing the nucleic acids is discharged out of the container.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**1. Claims 1, 2, 9, 12, 14, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullis (U.S. 5,187,083) in view of Tam (U.S. 5,741,647).**

Regarding Claim 1, Mullis discloses a method for separating and purifying a nucleic acid comprising the step of: adsorbing and desorbing a nucleic acid to and from a membrane of an organic macromolecule (Example 1, Col. 7-8).

Specifically, Mullis teach the capture and elution of DNA from blood on cellulose acetate membrane filters (Col. 7, line 45), which are organic macromolecules.

Regarding Claim 2, cellulose acetate inherently has hydroxyl groups on the surface thereof.

Regarding Claim 9, the nucleic acid is in a sample solution (a lysis solution of human blood; Col. 7, lines 34-40).

Regarding Claim 12, Mullis discloses washing the membrane with a nucleic acid washing buffer after adsorbing and then desorbing the nucleic acid from the membrane with a solution capable of desorbing the nucleic acid from the membrane. Specifically, the filter is washed with SDS/PBS solution and Tris chloride after adsorption (Col. 7, lines 46-51), and then the nucleic acid is desorbed using another aliquot of Tris chloride (Col. 7, lines 54-57).

Regarding Claim 14, the desorbing solution has a salt concentration of 0.5 M or less (Col. 7, lines 54-55).

Regarding Claim 15, Mullis discloses an example wherein the adsorption and desorption of the nucleic acid is performed within a vacuum-filtration device which is a container with at least two openings and which contained a cellulose acetate membrane filter (Example 3).

Regarding Claim 16, Mullis discloses a method wherein adsorption and desorption of the nucleic acid is performed by use of a unit for isolation and purification comprising (a) a membrane of the organic macromolecule; (b) a container having at least two openings and containing the membrane; and (c) a differential pressure generator connected to one opening of the container. Specifically, Mullis teaches an example wherein the adsorption and desorption of the nucleic acid is performed within a vacuum-filtration device which is a container with at least two openings and which contained a cellulose acetate membrane filter (Example 3). Further, the vacuum filtration device would inherently be connected to a differential pressure generator (i.e. the vacuum) which is connected to an opening of the device.

Mullis does not specifically teach the use of a membrane with a thickness of 10μm to 500μm.

Tam discloses a flow-through nucleic acid hybridization method using a flow-through mechanism by which the target nucleic acid molecules pass through a membrane having a thickness of about 160 microns (Column 2, Lines 25-35) allowing the single-stranded DNA to come in close contact with the corresponding capture

complementary DNA or RNA sequences immobilized inside the membrane pores so that the target sequence can be effectively detected in high sensitivity and specificity (Column 2, Lines 25-35; Columns 10-14, Examples I-VI).

Based on the disclosure of Tam, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing the methods of Mullis with a membrane thickness of 10μm to 500μm. The motivation to do so, provided by Tam, would have been to bring the nucleic acid sample in close contact with the organic macromolecules of the membrane in order to separate the nucleic acid sample with high sensitivity and efficiency. It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to practice the methods as claimed.

**2. Claims 1,2, 9, 10, 12, 13, 14, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodard (EP 0512767) in view of Tam (U.S. 5,741,647).**

Regarding Claim 1, Woodard discloses a method for separating and purifying a nucleic acid comprising the step of: adsorbing and desorbing a nucleic acid to and from a membrane of an organic macromolecule (p. 3, lines 19-30 and Example 6, p. 9).

Specifically, Woodard discloses the capture and elution of DNA from samples onto hydrophilic surfaces including nitrocellulose (p. 3, lines 49-50), which is an organic macromolecule.

Regarding Claim 2, nitrocellulose inherently has hydroxyl groups on the surface thereof.

Regarding Claim 9, the nucleic acid is in a sample solution (p. 4, lines 7-10).

Regarding Claim 10, Woodard discloses steps of treating a sample containing a cell or a virus with a nucleic acid solubilizing reagent (i.e. a lysis buffer) and then preparing the sample solution by adding an aqueous organic solvent to the solution. Specifically, Woodard discloses that DNA is obtained in such a way that the procedure ends with a suspension of DNA in a solution such as a lysate, a step which inherently includes treating the sample with a solubilizing reagent (p. 3, lines 3-13). Woodard discloses the subsequent addition of an organic solvent to the solution (p. 3, lines 19-22).

Regarding Claim 12, Woodard discloses washing the solid phase with a nucleic acid washing buffer after adsorbing and then desorbing the nucleic acid from the membrane with a solution capable of desorbing the nucleic acid from the membrane. Specifically, Woodard teach a step referred to as the "wash step" and suggest wash buffers (p. 3, lines 24-25), and then Woodard teaches that the nucleic acid is desorbed using an elution buffer (p. 3, lines 27-28).

Regarding Claim 13, Woodard discloses a nucleic acid washing buffer that contains 50% ethanol, for example (p. 3, line 24).

Regarding Claim 14, the desorbing solution has a salt concentration of 0.5 M or less (p. 3, lines 27-28).

Regarding Claims 15 and 16, Woodard discloses the use of a unit for isolation and purification that has a container with two openings that contains the membrane and is attached to a differential pressure generator. Namely, Woodard teaches the use of a blotter that "pulls" liquid through a membrane (p. 9, lines 5-15).

Woodard does not specifically teach the use of a membrane with a thickness of 10μm to 500μm.

Tam discloses a flow-through nucleic acid hybridization method using a flow-through mechanism by which the target nucleic acid molecules pass through a membrane having a thickness of about 160 microns (Column 2, Lines 25-35) allowing the single-stranded DNA to come in close contact with the corresponding capture complementary DNA or RNA sequences immobilized inside the membrane pores so that the target sequence can be effectively detected in high sensitivity and specificity (Column 2, Lines 25-35; Columns 10-14, Examples I-VI).

Based on the disclosure of Tam, one of ordinary skill in the art at the time of invention would have had a reasonable expectation of success practicing the methods of Woodard with a membrane thickness of 10μm to 500μm. The motivation to do so, provided by Tam, would have been to bring the nucleic acid sample in close contact with the organic macromolecules of the membrane in order to separate the nucleic acid sample with high sensitivity and efficiency. It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to practice the methods as claimed.

**3. Claims 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodard (EP 0512767) in view of Tam (U.S. 5,741,647), in further view of Morishita *et al.* (U.S. 4,118,336).**

Regarding Claims 3-7, the methods of Woodard have been outlined in the above rejections. Woodard does not teach a method wherein the high polymer is surface-saponified cellulose acetate or surface-saponified cellulose triacetate.

Regarding Claims 3 and 4, Morishita et al. teach surface saponified cellulose diacetate and triacetate particles and suggest using these for purification of nucleic acids (Col. 9, lines 6-7; Col. 9, line 16; Col. 10, line 7).

Regarding Claims 5 and 6, Morishita et al. teach surface saponified cellulose acetate particles wherein the saponification rate is 10% or more. For example, turning to example 1, the acetylation degree before saponification was 54.1% but less than 0.4% after saponification (Col. 9, lines 35-36).

Regarding Claim 7, the cellulose layer on the microparticles is a porous membrane, inherently.

It would have been *prima facie* obvious to one of ordinary skill in the art to have used the columns packed with surface saponified cellulose triacetate taught by Morishita et al. in the nucleic acid purification methods taught by Woodard. One would have been motivated to use the particles taught by Morishita et al. in view of the teachings of Woodard that binding matrixes suitable for use in their invention include any hydrophilic surface, and they specifically mention particles as an option (p. 3, lines

49-52). Morishita et al. provide such a surface, and specifically suggest the use of the surface for the extraction and purification of nucleic acids (Col. 9, lines 6-7). It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to practice the methods as claimed.

**4. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Woodard (EP 0512767) in view of Tam (U.S. 5,741,647), in further view of Benjamin et al. (U.S. 5,695,946).**

Regarding Claim 11, the methods of Woodard have been outlined in the above rejections. Woodard teaches using "typical" procedures for obtaining DNA from samples (p. 3, lines 5-6). Woodard does not specifically disclose a step wherein the nucleic acid solubilizing reagent comprises a guanidine salt, a surfactant, and a protease.

Benjamin et al. teach that target nucleic acid molecules are released from cells by treatment with any number of reagents, including guanidine salts, proteinase K and detergents (Col. 8, lines 7-12). Benjamin et al. exemplify the use of the surfactant SDS for cell lysis (Col. 12, line 15).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods taught by Woodard so as to have utilized a lysis buffer that included reagents that are typically considered lysis agents for the release of nucleic acids from sample cells. One would have been

motivated by the teachings of Woodard that any such typical methodologies for obtaining lysis solutions could be used and by the teachings of Benjamin *et al.* that each of these reagents are commonly used for the lysis of cells. It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to practice the methods as claimed.

**Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodard (EP 0512767) in view of Tam (U.S. 5,741,647), in further view of Heath et al. (WO 99/13976).**

Regarding Claim 17 and 18, the methods of Woodard have been outlined in the above rejections. Woodard does not specifically disclose the sequence of steps required in claims 17 and 18 wherein fluids are brought into contact with the solid support by inserting one opening of a unit for isolation and purification into a fluid (first sample, second washing buffer, third desorbing solution), creating a reduced pressure in a container by a differential pressure generator to suck the fluid into the chamber and into contact with the hydroxyl group, and creating an increased pressure within the chamber which results in discharge of the fluid from the chamber. Claim 17 requires the repetition of these steps for three different fluids, while claim 18 requires the repetition of these steps for only the sample and the desorbing solution.

Heath discloses methods for isolation of nucleic acid from samples and teaches automated steps of loading a sample into a container with at least two openings (p. 7,

lines 11-12), loading a wash into the container (p. 7, lines 13-17), and loading desorbing buffer (referred to as elution buffer) into the container (p. 7, lines 18-23). Heath discloses the use of vacuum pumps for the movement of solutions into and out of the isolation chamber (p. 8, lines 6-14; 21-22). Heath specifically teach that methods in which the sample is loaded via aspiration which occurs via the insertion of the opening of the chamber into the sample and the application of negative pressure to suck the sample into the chamber (p. 10, exemplified p. 23). Further, Heath teaches methods in which the gases are pumped into the chamber which increases pressure in the chamber and forces fluid out of the chamber (p. 12, lines 13-15).

Thus, in view of the teachings of the prior art, it would have been *prima facie* obvious to one of ordinary skill in the art to have applied the sample processing methodologies taught by Heath *et al.* to the methods taught by Woodard or the sample processing methods taught by Woodard in view of Morishita. One would have been motivated to have applied these methodologies for the processing of samples taught by Woodard or by Woodard in view of Morishita in order to have provided methods for applying the fluids necessary to practice the methods taught by Woodard to the solid supports for the isolation of nucleic acids. One would have been motivated to apply the methods taught by Heath et al. in order to take advantage of the potential for automation of sample processing. It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to practice the methods as claimed.

***Conclusion***

**No claims allowed. No claims are free of the prior art.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
9/15/05

Christopher M. Babic
Patent Examiner
AU 1637